R jection Under 35 USC §102(a)

Claims 1-4 and 7 have been rejected under 35 USC § 102(a) as being anticipated by Katoh et al (WO 00/04020). Applicant respectfully disagrees with this rejection as being improper since the effective priority filing date of this application is that of the provisional application on December 8, 1999, which is prior to the publication date for the Katoh reference of January 27, 2000. Since the Katoh reference is a PCT publication, and not a U.S. patent based on a PCT application, it is only entitled as a prior art reference to its publication date (see MPEP 715).

Therefore, it is respectfully submitted this rejection is improper and should be withdrawn.

Rejection Under 35 USC § 103(a)

Claims 1-4 and 7-9 have been rejected under 35 USC § 103(a) for obviousness over the same Katoh et al reference. For the same reasons stated above in the rejection under 35 USC § 102(a), it is respectfully submitted this rejection is improper and also should be withdrawn.

As suggested by the Examiner, a sentence has been added at page 1, line 1, of the specification to indicate continuity of the present application from the earlier filed U.S. Provisional Application.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with Markings to Show Changes Made."**

In view of the above amendments and remarks, it is respectfully submitted this case is in condition for allowance and early and favorable action is respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at line 1 of page 1 has been added as follows:

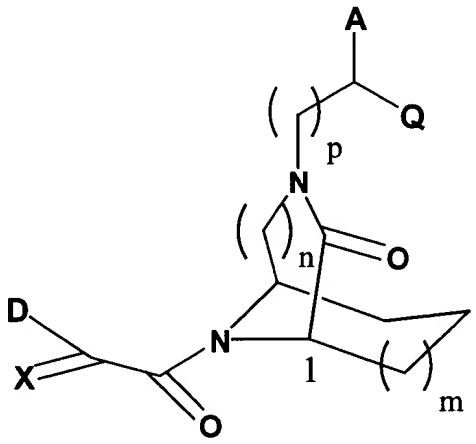
CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application No. 60/169,600, filed December 8, 1999.

In the Claims:

Claims 5 and 6 have been deleted. Claims 1-2 and 7-9 have been amended as follows:

1. (Amended) A compound having the formula (I)



(I)

or ~~and~~ pharmaceutically acceptable salts thereof, wherein:

X is O or F_2;

n is 1 ~~or 2~~;

m is 1 ~~0, 1, or 2~~;

p is 0 or 1;

wherein the stereochemistry at carbon position 1 is R or S;

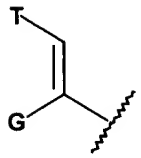
D is (C_1-C_6)-straight or branched alkyl, (C_2-C_6)-straight or branched alkenyl, (C_5-C_7)-cycloalkyl or (C_5-C_7)-cycloalkenyl substituted with (C_1-C_4)-straight or branched alkyl or (C_2-C_4)-straight or branched alkenyl, O-(C_1-C_4)-straight or branched alkyl, O-(C_2-C_4)-straight or branched alkenyl, 2-indolyl, 3-indolyl, (((C_1-C_4)-alkyl or (C_2-C_4)-alkenyl)-Ar or Ar;

Ar is a carbocyclic aromatic group selected from the group consisiting of phenyl, 1-naphthyl, 2-naphthyl, indenyl, azulenyl, fluorenyl, and anthracenyl; or a heterocyclic aromatic group selected from the group consisting of 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazinyl, 1,3,5-trithianyl, indolizinyl, indolyl, isoindolyl, 3H-indolyl, indolinyl, benzo[b]furanyl, benzo[b]thiophenyl, 1H-indazolyl, benzimidazolyl, benzthiazolyl, purinyl, 4H-quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, and phenoxazinyl;

Ar may contain one to three substituents which are independently selected from the group consisting of hydrogen, halogen, hydroxyl, hydroxymethyl, nitro, trifluoromethyl, trifluoromethoxy, (C_1-C_6)-straight or branched alkyl, (C_2-C_6)-straight or branched alkenyl, O-[((C_1-C_4)-straight or branched alkyl)], O-benzyl, O-phenyl, 1,2-methylenedioxy, amino, carboxyl, N-[((C_1-C_5)-straight or branched alkyl or (C_2-C_5)-straight or branched alkenyl)] carboxamides, N,N-di-[((C_1-C_5)-straight or branched alkyl or (C_2-C_5)-straight or branched alkenyl)] carboxamides, N-morpholinecarboxamide, N-benzylcarboxamide, N-thiomorpholinocarboxamide, N-picolinoylcarboxamide, O-W, CH_2-$(CH_2)_q$-W, O-$(CH_2)_q$-W, $(CH_2)_q$-O-W, and CH=CH-W;

W is 4-methoxyphenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrazyl, quinolyl, 3,5-dimethylisoxazoyl, isoxazoyl, 2-methylthiazoyl, thiazoyl, 2-thienyl, 3-thienyl, or pyrimidyl; q is 0-2;

Q and A are independently hydrogen, Ar, (C_1-C_{10})-straight or branched alkyl, (C_2-C_{10})-straight or branched alkenyl or alkynyl, (C_5-C_7)-cycloalkyl substituted (C_1-C_6)-straight or branched alkyl, (C_2-C_6)-straight or branched alkenyl or alkynyl, (C_5-C_7)-cycloalkenyl substituted (C_1-C_6)-straight or branched alkyl, (C_2-C_6)-straight or branched alkenyl or alkynyl, or Ar-substituted (C_1-C_6)-straight or branched alkyl, (C_2-C_6)-straight or branched alkenyl or alkynyl wherein, in each case, any one of the CH_2 groups of said alkyl, alkenyl or alkynyl chains may be optionally replaced by a heteroatom selected from the group consisting of O, S, SO, SO_2, N, and NR, wherein R is selected from the group consisting of hydrogen, (C_1-C_4)-straight or branched alkyl, (C_2-C_4)-straight or branched alkenyl or alkynyl, and (C_1-C_4)-bridging alkyl wherein a bridge is formed between the nitrogen and a carbon atom of said heteroatom-containing chain to form a ring, and wherein said ring is optionally fused to an Ar group; or



;

G is hydrogen, (C_1-C_6)-straight or branched alkyl or (C_2-C_6)-straight or branched alkenyl or alkynyl; and

T is Ar or substituted 5-7 membered cycloalkyl with substituents at positions 3 and 4 which are independently selected from the group consisting of oxo, hydrogen, hydroxyl, O-(C_1-C_4)-alkyl, or O-(C_2-C_4)-alkenyl.

2. (Amended) A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

m is ~~0 or~~ 1;

n is 1;

p is 1;

X is O or F_2;

D is 3, 4, 5-trimethoxyphenyl or t-pentyl;

Q and A are independently hydrogen; 2, 3, or 4-pyridyl; or phenyl-substituted (C_1-C_6)-straight or branched chain alkyl, wherein phenyl is optionally substituted with one to three substituants independently selected from (C_1-C_6) alkyl, O-(C_1-C_6) alkyl, carboxyl and trifluoromethyl, wherein said alkyl is straight or branched.

5. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

X is O;

m is 1;

n is 0;

p is 1;

A is 3-phenylpropyl, 2-phenylethyl, 2-(3,4-dimethoxyphenyl)ethyl, 3-(3,4,5-trimethoxyphenyl)propyl or 3-(3,4-dimethoxyphenyl)propyl; and

Q is 3-phenylpropyl, 2-phenylethyl, 3-(3,4,5-trimethoxyphenyl)propyl, 2-(3,4-dimethoxyphenyl)ethyl or 3-(3,4-dimethoxyphenyl)propyl.

6. A compound of claim 1 wherein:

the stereochemistry at carbon 1 is S;

X is O;

m is 1;

n is 0;

p is 0;

A is hydrogen; and

Q is 2-(3,4,5-trimethoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 3-(3,4-dimethoxyphenyl)propyl, 2-phenylethyl, 3-phenylpropyl, 4-phenylbutyl or

2-(3-pyridyloxy)ethyl.

7. (Amended) A pharmaceutical composition which comprises as an active ingredient an amount of a compound as claimed in any one of claims 1 to 4 ~~6~~, or a pharmaceutically acceptable salt thereof, effective for stimulating neurite growth in nerve cells, and one or more pharmaceutically acceptable carriers, excipients or diluents thereof.

8. (Amended) A method for stimulating neurite growth in nerve cells comprising the step of contacting said nerve cells with a composition comprising a neurotrophic amount of a compound with affinity for an FK506 binding protein as claimed in any one of claims 1-4 ~~6~~.

9. (Amended) A method for stimulating neurite growth in nerve cells comprising the step of contacting said nerve cells with a composition comprising a neurotrophic amount of a compound with affinity for FKBP12 as claimed in any one of claims 1-4 ~~6~~.